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SESQUITERPENE LACTONES FROM *PULICARIA SICULA**

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Key Word Index—*Pulicaria sicula*, Compositae, sesquiterpene lactones, guaianolides, xanthanolides

Abstract—The aerial parts of *Pulicaria sicula* afforded the known xanthanolides **1**–**6**, the guaianolides **7** and **8** as well as two new ones, the lactone **9** and the corresponding epoxide **10**. Furthermore nerylisobutyrate and the thymol derivatives **11** and **12** were present. The structures were elucidated by high field ^{1}H NMR spectroscopy and by partial synthesis of the epoxide **10**.

INTRODUCTION

From the genus *Pulicaria* (Compositae, tribe Inuleae, subtribe Inulinae) so far 13 species have been investigated chemically. Several species afforded diterpenes [1–4], thymol derivatives [5–8], caryophyllene derivatives [6–8] and flavones [9, 10]. The roots usually contain tridecapentaynene and trideca-tetraynediene [6]. However, *P. crispa* Sch. Bip. (= *Francoeuria crispa* Cass.) gave xanthanolides [11]. We now have studied the aerial parts of *P. sicula* (L.) Moris. The results are discussed in this paper.

*Part XIV. Constituents of plants growing in Qatar.

RESULTS AND DISCUSSION

From the roots of *P. sicula* (L.) Moris the isolation of widespread polyynes has been reported [5]. We now have studied the aerial parts which were collected in Qatar in spring 1987. After careful separations finally nerylisobutyrate, the thymol derivatives **11** [12] and **12** [13], the xanthanolides **1** [14], **2** [15], **3** [16], **4** [16], **5** [17] and **6** [18], the guaianolides **7** [19] and **8** [20] as well as **9** and **10** were obtained.

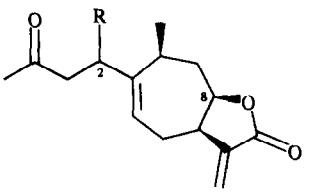
The structures of **1**–**8** were determined by high field ^{1}H NMR spectroscopy and/or by comparing the spectra with those of authentic material or with the data in the literature.

The molecular formula of **9** ($C_{15}H_{20}O_3$) already indicated that this lactone might be an isomer of **7** and **8**.

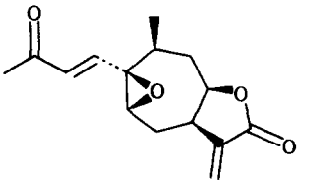
Table 1. ^{1}H NMR spectral data of **9** and **10** (400 MHz, δ values)

H	**9** $CDCl_3$	**9** $CDCl_3/C_6D_6$ (1:1)	**9** C_6D_6	**10** $CDCl_3$	**10** C_6D_6	Multiplicity
2	5.38	5.10	5.08	3.62 *br s*	2.97 *br s*	*ddt*
3 }	2.38 *br s*	2.16	2.24	2.08	1.82	*br d*
3′ }		2.09	2.10	1.78	1.22	*br d*
5	2.40	2.05	2.07	2.04 *dd*	1.68 *dd*	*br d*
6α	2.00 *m*	1.63	1.58	1.81	1.24	*ddd*
6β	1.41	1.07	1.03	1.41	0.72	*ddd*
7	3.31	2.77	2.58	3.25	2.34	*ddddd*
8	4.76	4.27	4.12	4.74	3.90	*ddd*
9α	2.00 *m*	1.72	1.67	2.09	1.58	*ddd*
9β	1.55	1.26	1.23	1.75	1.17	*ddd*
10	2.22	1.80	1.66	2.16	1.48	*br ddq*
13	6.26	6.14	6.23	6.32	6.21	*d*
13′	5.61	5.18	5.00	5.69	4.98	*d*
14	1.24	1.00	0.94	0.95	0.62	*d*
15	1.32	1.06	1.09	1.22 *d*	1.10 *d*	*s*
OH	1.88		1.37	3.73	3.81	*br s*

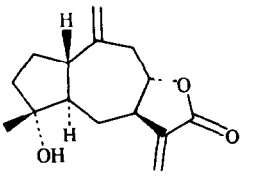
J [Hz]: 2,3 = 2.5, 2,3′ = 2,5 = 2,10 ~ 1.5, 3,3′ = 16, 5,6α = 2, 5,6β = 6β,7 = 12, 6α,6β = 13, 6α,7 = 4, 7,8 = 8, 7,13 = 3, 7,13′ = 2.5, 8,9α = 4, 8,9β = 12, 9α,9β = 13, 9α,10 = 1.5, 9β,10 = 12 (compound **10**: 2,3 = 2.3′ ~ 0.5, 3,3′ = 14, 5,6α = 6α,7 = 2.5, 5,6β = 12.5, 8,9α = 4.5, 9α,10 = 1.5, OH = 1).



	1	2	3	4	5
R	H	H	OH	OH	H
		8βH		8βH	Δ^2



6



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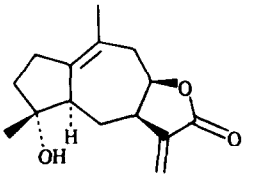

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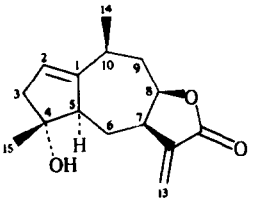

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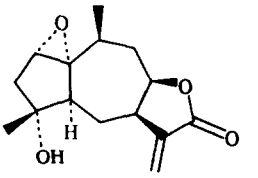

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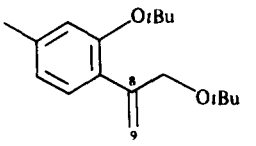

11

12 8,9-epoxide

Comparison of the ^{1}H NMR spectra (Table 1) showed that indeed a hydroxyguaianolide with two double bonds was present The spectrum in deuteriochloroform showed several overlapping signals. But all signals could be assigned by spin decoupling in deuteriobenzene and in a mixture with chloroform. The resulting sequences clearly indicated that a 1,2-double bond was present Furthermore the observed couplings established the configuration at C-10 while that at C-4 was deduced from the chemical shifts of H-5 and H-6 which were deshielded by the 4α-hydroxy group. This was supported by the configuration of **10** (see below)

The structure of **10** was also deduced from the ^{1}H NMR spectra in different solvents (Table 1) Especially in deuteriobenzene a complete assignment of all signals was possible. As in estafiatin, only a very small vicinal coupling between the epoxide proton and the neighbouring methylene protons (H-3) were observed A *W*-coupling between H-15 and the hydroxy proton caused a doublet splitting of the signal of the former The configurations at C-7, C-8 and C-10 followed from the observed couplings if a model was inspected, while the configuration of the epoxide could not be determined directly. However, epoxidation of **9** afforded only one product which was identical with the natural product **10** Inspection of a model showed that this result only agrees with the attack from the α-face The configurations at C-1, C-2 and C-4 followed from a hydrogen bond in the ir

(3500 cm^{-1}) and were established by NOE's between H-14 and H-2 as well as between H-15 and H-6α.

The isolation of the xanthanolides **1–6** and the guaianolides **7–10** may be an indication that *P. sicula* is related to *P. crispa* which afforded very similar constituents. The presence of thymol derivatives is less important as these compounds are widespread in the whole subtribe.

EXPERIMENTAL

The air-dried aerial parts (250 g, collected during February 1987 in Qatar, voucher deposited in the Herbarium of the University of Qatar) were extracted with Et_2O–MeOH–petrol, 1:1:1, and the extract obtained was separated as reported previously [21]. CC fractions were combined into four parts (1: Et_2O–petrol, 1:9; 2: Et_2O–petrol, 1:3; 3: Et_2O; and 4: Et_2O–MeOH, 9:1). TLC of fraction 1 (silica gel, PF 254, Et_2O–petrol, 1:9) gave 20 mg **11** and 10 mg **12**. TLC of fraction 2 (Et_2O–petrol, 1:3) gave 30 mg neryisobutyrate and TLC of fraction 3 (Et_2O–petrol, 1:1) afforded 280 mg **2** and 220 mg **1** (less polar). HPLC of fraction 4 (RP 18, MeOH-H_2O, 13:7, *ca* 100 bar) afforded 10 mg **8** (R_t 6.0 min) and two mixtures (4/2, R_t 1.5 min and 4/3, R_t 3.0 min). Fraction 4/2 gave by TLC ($CHCl_3$–C_6H_6–Et_2O–MeOH, 20:20:10:1) 4 mg **5** (R_f 0.80), 1 mg **6** (R_f 0.62), 2 mg **10** (R_f 0.60), 2 mg **4** (R_f 0.50) and 4 mg **3** (R_f 0.40). TLC of fraction 4/3 (Et_2O, two developments) gave 40 mg **7** (R_f 0.62) and 20 mg **9** (R_f 0.55).

1,2-Dehydro-1,10α-dihydropseudoivalin (**9**). Colourless crystals, mp 112°, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1770 (γ-lactone), MS *m/z* (rel. int.): 248.141 $[M]^+$ (7) (calc. for $C_{13}H_{20}O_3$: 248.141), 230 $[M-H_2O]^+$ (42), 215 $[230-Me]^+$ (12), 206 (20), 190 (47), 119 (100), 91 (60), $[\alpha]_D^{24}$ +6 ($CHCl_3$, *c* 1.53).

To 10 mg **9** in 2 ml $CHCl_3$ 20 mg *m*-chloroperbenzoic acid and 10 mg K acetate were added. After 30 min stirring, usual work-up afforded 10 mg **10**, identical with the natural lactone *1α,2α-Epoxy-1,10α-dihydropseudoivalin* (**10**). Colourless crystals, mp 173°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH, hydrogen bonded), 1770 (γ-lactone), MS *m/z* (rel. int.): 264.136 $[M]^+$ (1) (calc. for $C_{15}H_{20}O_4$: 264.136), 249 $[M-Me]^+$ (7), 246 $[M-H_2O]^+$ (6), 231 $[246-Me]^+$ (9), 221 (12), 206 (26), 204 (25), 166 (70), 108 (100), 95 (98), $[\alpha]_D^{24}$ +60 ($CHCl_3$, *c* 0.08).

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